26. (Amended) The composition of claim 22 [further comprising a] wherein said hapten is selected from the group consisting of dinitrophenyl, trinitrophenyl, and N-iodoacetyl-N'-(5 sylfonic 1-naphtyl) ethylene diamine.

Claim 28, line 1, following "claim", delete "22", insert therefor --38--.

REMARKS

Applicant hereby requests an interview pursuant to 37 C.F.R. §1.133(a) prior to issuance of the next Office Action. The Examiner's attention is directed to the telephone number of the undersigned appearing on the last page of the instant response.

Claims 2-10, 22-28, and new claims 34-38 are pending in the above-identified application. Support for the amendments and newly added claims may be found in the specification as filed, see for example, page 8, lines 4-6 and 13-22; page 9, lines 15-28; page 10, lines 1-10; page 11, lines 5-13 and 26-27; page 13, lines 9-12; page 15, lines 3-9; page 18, lines 3-6. Claims 1 and 29-33 are cancelled.

Claims 22-31, restriction requirement Group IV, were elected and examined with claims 1-10 of restriction requirement Group I. Accordingly, the claims as amended together with the newly added claims are part of the Groups elected for prosecution in response to the restriction requirement.

The specification is objected to and claims 1-7, 10, and 22-33 are rejected pursuant to 35 U.S.C. §112, first paragraph and second paragraph. There is no prior art rejection of the claims. The objections and rejections are considered in view of the claims as amended, and claims 34-38 newly added.

THE PRESENT INVENTION

The present invention is directed to a pharmaceutical composition comprising a hapten modified human tumor cell. The tumor cell may be selected from the group consisting of melanoma, breast, lung, colon, breast, kidney, and prostate. The hapten may be selected from the group consisting of dinitrophenyl, trinitrophenyl, and N-iodoacetyl-N'-(5 sylfonic 1-naphtyl) ethylene diamine. The composition of the present invention may be further combined with a carrier such as saline solution and culture medium. A method of treating cancer comprising administering a composition comprising a hapten modified tumor cell is also embodied by the present invention.

THE OBJECTION AND REJECTION PURSUANT TO 35 U.S.C. §112, FIRST PARAGRAPH

The objection to the specification and the rejection of claims 1-7, 10, and 22-33 pursuant to 35 U.S.C. §112, first paragraph, as failing to adequately teach how to make and/or use the invention, for failing to provide an enabling disclosure, is maintained. The objection and rejection are directed to the alleged failure of the specification to teach how to select tumor cells or extracts which would be effective in treating cancers other than melanoma, see Office Action dated December 22, 1995, page 5, lines 6-9.

The present invention is directed to a composition comprising haptenized tumor cells and method of treating cancer comprising administering the composition. The selection of melanoma cells effective in treating melanoma is set forth in the specification as filed, see above first paragraph following "REMARKS" in support of the amendments and newly added

claims. Further to the support for the enabling disclosure of how to make and use the invention in the application as filed, provided herewith is a Declaration of Dr. David Berd.

A declaration of a person skilled in art addressing a question of fact should be considered by the Examiner. *In re Alton*, 37 USPQ2d 1578 (Fed. Cir. 1996), citing *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 227 USPQ 657, 665 (Fed. Cir. 1985).

> [U]se of the words "it is my opinion" to preface what someone of ordinary skill in the art would have known does not transform the factual statements contained in the declaration into opinion testimony.

Alton at 1583.

Dr. Berd provides facts supporting the enabling disclosure in the application for a composition comprising a haptenized tumor cell and method of administering the composition for the treatment of cancer. He provides facts in support of melanoma representing other tumors in general. As a result, skilled artisans expect the composition of the present invention comprising tumor types other than melanoma to be equivalent to melanoma in treating other cancers.

Dr. Berd, as a skilled artisan, also attests to the recognition that dinitrophenyl is representative of haptens in general. Accordingly, skilled artisans find dinitrophenyl to be equivalent to other haptens and other haptens are expected to perform equivalently to dinitrophenyl in the composition of the present invention.

Thus, the specification as filed meets the requirements of 35 U.S.C. §112, first paragraph. Accordingly, Applicant respectfully requests withdrawal of the rejection in view of the remarks set forth above.

THE REJECTION PURSUANT TO 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-7, 10, and 22-33 are rejected, as being indefinite for failing to particularly point out and distinctly claim the invention, under 35 U.S.C. §112, second paragraph. The rejection is directed to the alleged vague language "tumor cell extracts comprising a peptide", "extracts of the present invention comprise a peptide isolated from cancerous cells", and "irradiated composition".

The present invention is directed to a composition comprising a haptenized tumor cell and method of treating cancer comprising administering the composition. This rejection is moot in view of the amendments to the claims. Accordingly, Applicant respectfully requests withdrawal of the rejection in view of the remarks set forth above.

THE OBJECTION AND REJECTION PURSUANT TO 35 U.S.C. §112, FIRST PARAGRAPH

The objection to the specification and the rejection of claims 1-7, 10, and 22-33 pursuant to 35 U.S.C. §112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure. The objection and rejection are directed to the alleged failure of the specification to teach the administration of an irradiated composition of tumor cell extracts comprising a peptide conjugated to a hapten or a

mixture of tumor cells and the above peptide, see Office Action dated December 22, 1995, page 9, lines 14-16.

The present invention is directed to a composition comprising a haptenized tumor cell and method of treating cancer comprising administering the composition. The selection of melanoma cells effective in treating melanoma and the representation of melanoma as equivalent to other tumor types is set forth in the specification as filed as well as in the Declarations filed herewith. The specification as filed meets the requirements of 35 U.S.C. §112, first paragraph, see first paragraph following "REMARKS" in support of the amendments and newly added claims.

Accordingly, Applicant respectfully requests withdrawal of the rejection in view of the remarks set forth above.

PRIOR ART

The claims are not rejected in view of prior art. In the interest of encouraging efficient prosecution, Dr. Berd's Declaration addresses references previously cited during prosecution of the present application as well as parent application 07/985,334 and grand parent application 07/520,649 in view of the claims as amended and newly added.

In re Alton specifically addresses the factual issue involved with a rejection under 35 U.S.C. §112, first paragraph. While the ultimate determination of obviousness is a question of law, the scope and content of the prior art, differences between the prior art and the claimed invention, the level of ordinary skill in the art, and objective evidence of secondary considerations of patentability are questions of fact. *Para-Ordnance Manufacturing*

Inc. v. SGS Importers International, 37 USPQ2d 1237, 1239 (Fed. Cir. 1995). What the prior art teaches and whether it teaches toward or away from the claimed invention also is a determination of fact. *Para-Ordnance* at 1239 citing *In re Bell*, 26 USPQ2d 1524, 1531 (Fed. Cir. 1993), citing *Raytheon Co. v. Roper Corp.*, 220 USPQ2d 592, 599-600 (Fed. Cir. 1983).

Dr. Berd addresses the patentability of the present invention in view of the Helper Hypothesis of Mitchison. The Helper Hypothesis provided that hapten priming generated a helper response specific for a particular hapten. While the Helper Hypothesis provided the basis for a number of cancer treatments, it is no longer believed to be responsible for an immune response in cancer. Rather, unmodified peptides associated with the major histocompatibility complex appear to be providing a reasonable explanation for immune responses in cancer patients.

Dr. Berd addresses his own prior attempts in the development of a composition for treating cancer that includes non-haptenized tumor cells. Patients treated with non-haptenized tumor cells were pretreated with cyclophosphamide which was believed to result in immunity. Non-haptenized tumor cells were not successful for the treatment of cancer.

Dr. Berd attests to the patentability of the present invention in view of the teachings of Fujiwara *et al.*, *J. Immunol.* **1980** *124*:863 (Fujiwara I); Fujiwara *et al.*, *J. Immunol.* **1984**, *132*:1571 (Fujiwara II); and Fujiwara *et al.*, *J. Immunol.*, **1984**, *133*:509 (Fujiwara III). Fujiwara I, II, and III differ from the present invention in three critical areas: spontaneous tumors, immunoprophylaxis, and local therapy. Dr. Berd, as a skilled artisan, provides reasons as to why the three areas do not teach or suggest the present invention.

Finally, Miller *et al.*, *J. Immunol* **1976** *117*:1519 is also discussed by Dr. Berd in the attached Declaration. Miller *et al.* simply do not administer a haptenized tumor cell.

CONCLUSION

In view of the foregoing remarks, Applicant respectfully requests reconsideration and allowance of all pending claims, claims 2-10, 22-28, and new claims 34-38. Early and favorable notification to that effect is earnestly solicited.

Respectfully submitted,

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DATE: 11/21/96

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